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The Interwoven Global Epidemics of Mercury Toxicity and Autism

By Robert F. Kennedy Jr.

In nature, toxic metals generally are bound with other elements rather than being present in their pure form. However, with the advent of large-scale industrial processes to extract metals from naturally occurring compounds, humans let the genie out of the bottle, contributing significantly to the distribution of mercury, aluminum and other heavy metals in the environment. When released from nature's semi-protective hold, these "invariably toxic" metals wreak havoc on living systems, including humans, animals and plants alike.

Modern-day scientists have been amassing evidence of mercury's toxicity for decades, with a growing focus in recent years on the metal's association with neurodevelopmental disorders, including autism spectrum disorder (ASD). A new review article in the multidisciplinary journal *Environmental Research* pulls together a wide body of literature with the aim of summing up current research and emerging trends in mercury toxicology. Geir Bjørklund, the study's lead author, is the founder of Norway's non-profit Council for Nutritional and Environmental Medicine and has published prolifically on topics related to heavy metals, autoimmune disorders and ASD.

Multiple avenues of exposure

Exposure to mercurial compounds remains widespread, despite feeble attempts to ban some uses. Bjørklund et al.'s review covers all three categories of mercury: elemental, organic and inorganic. Exposure to volatile *elemental* mercury can come about as a result of occupational contact or vapor from dental amalgam fillings. *Organic* mercury—the most frequent form of exposure, according to Bjørklund and colleagues—exists as methylmercury (in fish) and ethylmercury (in the vaccine preservative thimerosal). Coal-fired power plants send *inorganic* mercury into the environment, where the toxic metal works its way up the marine food chain.

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Interconversion between various forms of mercury also occurs. For example, elemental and organic mercury can cross the blood-brain barrier and bioaccumulate in the form of inorganic mercury. Studies also have described “mixed exposure” in the brain to both organic and inorganic mercury compounds. Because mercury plays no constructive metabolic role whatsoever, humans have not evolved effective mechanisms to excrete it. Children with ASD have a particularly hard time detoxifying and excreting mercury.

Multiple mechanisms of toxicity

Mercury exerts toxicity through a number of different mechanisms and has effects at both the molecular and cellular levels. For their purposes, Bjørklund and coauthors zero in on eight interrelated mechanisms, although there are others. Every single one of the toxic mechanisms that they describe has a documented association with ASD.

- **Sulfur:** A key and widely recognized fact about mercury is that it is “thiophilic,” meaning that it has an affinity for biochemically important sulfur compounds called thiols. Mercury binds to the sulfur-containing amino acid cysteine (which contains a thiol group); this allows mercury to piggy-back into brain cells and other target cells through a phenomenon known as molecular mimicry (meaning that the problematic mercury-cysteine entity “mimics” the useful amino acid methionine). According to leading toxicologists at the Centers for Disease Control and Prevention (CDC), mercury then “blocks or attenuates [the] protein molecule’s range of availability for normal metabolic function.” Mercury also reduces sulfate absorption. Individuals with ASD frequently have low levels of sulfate.
- **Immune activation and autoimmunity:** Bjørklund et al. outline numerous mercury-related immune system effects, including “immunostimulation, immunosuppression, immunomodulation, delayed-type hypersensitivity..., and autoimmunity.” These effects occur largely due to mercury’s influence on immune cytokines—proteins that are important in helping cells

communicate. Chronic elevation of inflammatory cytokines and other immune abnormalities such as activation of microglia (immune cells in the brain) are hallmarks of both mercury exposure and ASD.

- **Protein synthesis:** Researchers have reported since the late 1960s that mercury inhibits protein synthesis (a fundamental cell process that involves both DNA and RNA), interfering with cells' ability to build new proteins. Bjørklund and coauthors report that inorganic mercury is particularly disruptive in this regard. Investigators have postulated that dysregulated protein synthesis, which disrupts the balance between excitation and inhibition in brain cells, plays a causal role in ASD.
- **Brain microtubules:** Neuropsychiatrist Jon Lieff describes microtubules as "the brains of the cell" and suggests that cerebral microtubules may be "the seat of consciousness." Microtubules form the scaffolding required by axons (nerve fibers that transmit neuronal signals). Mercury preferentially targets axonal microtubules, leading to their "depolymerization and derangement," according to the *Environmental Research* authors. Moreover, mercury is unique among toxic metals in having these microtubule effects. Axonal disturbances and the altered brain connectivity that these disturbances promote are widely documented features of ASD.
- **Membrane transport:** Cell membrane transport refers to the process whereby molecules (such as amino acids) pass into or out of a cell. Mercury can disturb amino acid transport and also "penetrate" across biological membranes. The authors note the need for "approaches to inhibit [mercury's] transfer both at the placental border and at the blood-brain barrier." An international research group recently described the relationship between ASD and impaired amino acid transport at the blood-brain barrier.
- **Glutathione:** Numerous researchers have described how organic mercury, in particular, impairs glutathione activity, thereby lessening protection from oxidative stress and weakening the body's detoxification capacity. The relationship is bidirectional, according to Bjørklund

and coauthors, because when brain glutathione levels drop, the uptake of mercury in brain tissue increases substantially. Lowered glutathione levels, elevated oxidative stress and a higher body burden of mercury have been repeatedly documented as core characteristics of ASD.

- **Metallothioneins:** Metallothioneins (MTs), a family of proteins, are antioxidants and metal chelators that work to maintain metal homeostasis. MTs also play an important role in neuroprotection and regeneration. Although MTs are present to “protect the brain and gastrointestinal tract against overload by toxic metals,” Bjørklund and coauthors cite evidence showing that common genetic mutations and variations in MTs may increase some individuals’ susceptibility to mercury-induced neurotoxicity, including individuals with ASD. Studies have identified “a significant increase in both metal content and metallothionein expression” in autistic children.
- **Zinc and copper:** Appropriate metabolism of zinc and copper is important for healthy neurological functioning. When mercury binds to metallothioneins, it can substitute for zinc and copper, “interact with [zinc] and [copper] availability” and thereby disturb the normal zinc-copper ratio. In a previous publication, Bjørklund described mercury’s role in disturbing zinc and copper metabolism and the typically low zinc-copper ratio in autistic children. Other researchers have measured the zinc-copper ratio in plasma as a biomarker for mercury toxicity in ASD children.

Reducing mercury toxicity

Bjørklund and coauthors also devote several paragraphs to a discussion of the essential trace element selenium, which plays an important antioxidant role, among other functions. The authors note that mercury is highly “selenophilic,” binding to selenium “with an extraordinarily high affinity... when compared with the affinity for sulfur.” The welcome implication spelled out by the authors—which has been known to researchers for nearly half a century—is that selenium has a “high capability...to reduce the toxicity of [mercury] compounds.” The authors list several mechanisms whereby selenium can minimize mercury-induced toxicity,

such as by improving mercury's excretion or sequestration and strengthening antioxidative activity. Autism researchers have identified "a significant elevation of [mercury]...together with a significant decrease in the [selenium] levels in [red blood cells] of patients with ASD when compared to...healthy controls." These researchers agree that selenium has an important role to play in reducing mercury toxicity in ASD patients.

Translating research into action

It has been over a decade and a half since a seminal publication in *Medical Hypotheses* described autism as "a novel form of mercury poisoning" and showed how "every major characteristic of autism has been exhibited in...cases of documented mercury poisoning." Ten years later, Kern and colleagues published a detailed consideration of "parallels between mercury intoxication and the brain pathology in autism" in *Acta Neurobiologiae Experimentalis*. A 2017 publication in *Molecular Neurobiology* by autism expert Dr. Richard Frye and others reviews "associations between mercury exposure and ASD subtypes," even "at doses well below the current reference levels considered to be safe." Thus, Bjørklund and coauthors are far from alone in synthesizing the evidence base and drawing attention to the global public health epidemics of mercury toxicity and autism.

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Last year, CDC toxicologists published a comprehensive review that specifically focused on the two forms of organic mercury. The CDC authors concluded that there are "many commonalities [and] similarities in the mechanisms of toxic action of methylmercury and ethylmercury," particularly regarding their association with neurotoxicity and neurodevelopmental disorders such as ASD. Both forms of organic mercury cause DNA damage (or impair DNA synthesis), affect cell division, decrease glutathione activity and increase oxidative stress, among other similar effects. These findings are particularly noteworthy in light of Bjørklund and coauthors' observation that "co-exposure with [ethylmercury] and [methylmercury] might induce more adverse neurotoxic effects than each agent alone." Bjørklund's team calls on researchers to actively investigate these additive toxicological effects.

At the end of the day, as noted by mercury expert Philippe Grandjean, there is a need to move beyond simply generating “endless replications” in the form of “thousands of toxicology publications every year” on mercury and other well-understood toxic metals. The Bjørklund team’s broad review of over 200 studies—including recent findings as well as articles dating back several decades—shows that we already know more than enough about mercury’s hazards to take decisive action.

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